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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,975	LI ET AL.	
	Examiner	Art Unit	
	Brandon J Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,22-25,31,32 and 43-45* is/are pending in the application.

4a) Of the above claim(s) *7-16,22-25,31,32,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The response filed on December 8, 2004 to the restriction requirement of September 8, 2004 has been received. Applicants have elected Group I, claims 1-6, as specifically drawn to an antibody that binds specifically to a polypeptide comprising an ubiquitination-regulating domain of TSG101 protein. Applicants have canceled claims 17-21, 26-30 and 33-36.

Applicant's election with traverse of Group I, claims 1-6, is acknowledged. The traversal is on the ground(s) that there is no undue search burden on the Examiner since all the claims in the instant application are related to agents and methods for modulating the interaction between TSG101 and MDM2. These arguments have been considered and not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the restriction requirement of September 8, 2004.

As to the question of burden of search, the inventions are classified differently, necessitating different searches of the US Patents and literature. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group.

For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-16, 22-25, 31-32 and 43-45 are currently pending.

Claims 7-16, 22-25, 31-32 and 44-45 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-6 and 43 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statements filed on 6/17/2002, 11/21/2003 and 12/08/2004 are acknowledged and have been considered considered. A signed copy of the IDS is attached hereto.

In addition, the listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 16 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-6 are rejected as vague and indefinite for reciting the term TSG101 as the sole means of identifying the claimed molecule. The use of laboratory designations only to identify a

particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify TSG101, for example, by SEQ ID NO. and function of TSG101.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of antibodies that bind to a genus of polypeptides comprising a ubiquitination domain and/or a functional fragment thereof referred to as TSG101. However, the written description in this case only sets forth antibodies which bind to one species of polypeptide comprising a ubiquitination domain referred to as human TSG101 consisting of the amino acid sequence set forth in SEQ ID NO: 1.

The specification teaches (page 12, 3rd paragraph) that specific polypeptides of the invention include, but are not limited to, any isolated polypeptide comprising a ubiquitination-regulating domain which regulates ubiquitination, e.g., via regulating conjugases (E2 enzymes). With regards to the ubiquitination-regulating domain, the specification teaches that ubiquitination-regulating domain not only includes an amino acid sequence of an ubiquitination-regulating domain of a TSG101 protein, but also any functional fragment of a ubiquitination-regulating domain of a TSG101 protein comprising amino acids 10-140, 20-140, 30-140, 40-140, 1-160 ... 50-250 or 1-250 of TSG101 (page 11, 4th paragraph to page 12, 2nd paragraph). However, the written description only reasonably conveys antibodies that bind to one species of polypeptide consisting of a ubiquitination domain referred to as human TSG101 consisting of the amino acid sequence set forth in SEQ ID NO: 1; and is not commensurate with the full scope of antibodies which bind to any and/or all polypeptides comprising a ubiquitination domain and/or a functional fragment thereof of a TSG101 protein. A

description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of TSG101 proteins that encompass the genus of polypeptides, nor does it provide a description of structural features that are common to the polypeptides. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one species of TSG101 protein is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Applicants should further refer to Example 13 of the revised interim Written Description

Guidelines regarding protein variant language (see http://www.uspto.gov/web/menu/written.pdf>).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only antibodies that bind to one species of polypeptide comprising a ubiquitination domain referred to as human TSG101 consisting of the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999).

In the instant case, the claims are drawn to an antibody that binds specifically to a polypeptide comprising an ubiquitination-regulating domain, wherein the ubiquitination-regulating domain is an ubiquitination-regulating domain of a TSG101 protein (claims 1-2). The claims are further drawn to wherein the TGS101 protein is a human TSG101 protein (claim 3). Furthermore, the ubiquitination-regulating domain is additionally limited to comprise amino acid residues 50-140, 1-140, or 140-250 of human TSG101 protein (claims 4-6).

Li. et al. teach antibodies which have been raised to normal or mutated forms of TSG101 (column 8, line 59-63). Specifically, the patent teaches antibodies that specifically recognize the coiled domain, leucine zipper and proline rich domains of TSG101 (column 8, lines 64 to column 9, line 4). With regards to TSG101, Li et al. provide both the mouse TSG101 and the human homolog (column 3, lines 26-38, see attached sequence comparison for human homolog sequence 4).

Although the reference does not specifically teach that the antibody binds to a polypeptide comprising a ubiquitination-regulating domain, the claims are drawn to the product *per se* and inherently, such an antibody would bind to a polypeptide comprising a ubiquitination-regulating domain. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-6 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999).

(Note: Due to the indefiniteness of the claims as set forth above, TGS101 protein (Claims 2-6) will be interpreted for art purposes as being the amino acid sequence set forth in SEQ ID NO: 1, See specification page 6, figure 6.)

Brie *et al.* teach a purified protein having an amino acid sequence having 100% identity to the amino acid sequence set forth in SEQ ID NO: 1 (Figures 1A-1B, see attached sequence comparison). The patent further teaches antibodies including, but not limited to, polyclonal, monoclonal and chimeric which bind specifically to the polypeptide (column 17, line 15 to column 18, line 16). Furthermore, Brie et al. disclose that the antibodies can be used as a pharmaceutical agent for the prevention and or treatment of disease associated with expression of the polypeptide (column 16, lines 56-60). Although the reference does not specifically teach that the antibody binds to a polypeptide comprising a ubiquitination-regulating domain, the claims are drawn to the product *per se* and inherently, such an antibody would bind to a polypeptide comprising a ubiquitination-regulating domain. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to

establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,835,816.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the species claimed within the conflicting patent would anticipate the genus claimed in the application being examined. For instance, the antibody that binds to a TSG101 protein as set forth in SEQ ID NO: 2 or SEQ IDNO: 4 claimed in the conflicting patent appears to fall within the same scope of an antibody that binds to a TSG101 protein in the application being examined and, therefore, a patent to an antibody that binds TSG101 protein would necessarily, extend the rights of an antibody that binds to a TSG101 protein as set forth in SEQ ID NOs: 2 or 4 should the application being examined issue as a patent after the conflicting patent.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

GARY NICKOL
PRIMARY EXAMINER